

WHAT IS CLAIMED IS:

1. An isolated nucleic acid molecule comprising a nucleotide sequence having at least an 80% identity to SEQ ID NO:3 or SEQ ID NO:5, or the complementary sequence thereof.
2. An isolated nucleic acid molecule encoding a polypeptide comprising an amino acid sequence having at least a 70% identity to SEQ ID NO:4 or SEQ ID NO:6, or the complementary sequence thereof.
3. An isolated nucleic acid molecule comprising at least 12 sequential bases of SEQ ID NO:3 or SEQ ID NO:5, or the complementary sequence thereof.
4. The isolated nucleic acid molecule of claim 2, comprising a nucleotide sequence encoding a cyclooxygenase-3 enzyme, wherein the enzyme comprises an amino acid sequence having at least about 70% amino acid sequence identity to SEQ ID NO:4 or SEQ ID NO:6, or the complementary sequence thereof.
5. The isolated nucleic acid molecule of claim 2, comprising a nucleotide sequence encoding a cyclooxygenase-3 enzyme wherein the enzyme comprises an amino acid sequence having at least about 80% amino acid sequence identity to SEQ ID NO: 4 or SEQ ID NO:6, or the complementary sequence thereof.

6. The isolated nucleic acid molecule of claim 2,
comprising a nucleotide sequence encoding a cyclooxygenase-
3 enzyme, wherein the enzyme comprises an amino acid
sequence having at least about 90% amino acid sequence
5 identity to SEQ ID NO: 4 or SEQ ID NO:6, or the
complementary sequence thereof.
7. The isolated nucleic acid molecule of claim 2,
comprising a nucleotide sequence encoding a cyclooxygenase-
10 3 enzyme wherein the enzyme comprises an amino acid
sequence of SEQ ID NO:4 or SEQ ID NO:6, or the
complementary sequence thereof.
8. The isolated nucleic acid molecule of claim 2,
15 comprising a nucleotide sequence encoding a cyclooxygenase-
3 enzyme wherein the enzyme comprises an amino acid
sequence of SEQ ID NO:9 or SEQ ID NO:11, or the
complementary sequence thereof.
- 20 9. The isolated nucleic acid molecule of claim 2,
comprising a nucleotide sequence of SEQ ID NO:3 or SEQ ID
NO:5, or the complementary sequence thereof.
10. The isolated and purified nucleic acid molecule of
25 claim 2, comprising a nucleotide sequence of SEQ ID NO:8 or
SEQ ID NO:10, or the complementary sequence thereof.
11. An expression vector comprising the nucleic acid
molecule of claim 1.
- 30 12. An expression vector comprising the nucleic acid
molecule of claim 2.

13. An expression vector comprising the nucleic acid molecule of claim 3.

5 14. A recombinant host cell comprising the expression vector of claim 11.

15. A recombinant host cell comprising the expression vector of claim 12.

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16. A recombinant host cell comprising the expression vector of claim 13.

15 17. A substantially purified polypeptide comprising an amino acid sequence having at least about 70% identity to SEQ ID NO:4 or SEQ ID NO:6, wherein said polypeptide is capable of converting arachidonic acid to prostaglandin H₂.

20 18. The substantially purified polypeptide of claim 17 comprising an amino acid sequence having at least about 80% identity to SEQ ID NO:4 or SEQ ID NO:6.

25 19. The substantially purified polypeptide of claim 17 comprising an amino acid sequence having at least about 90% identity to SEQ ID NO:4 or SEQ ID NO:6.

20. The substantially purified polypeptide of claim 17 comprising an amino acid sequence of SEQ ID NO:4 or SEQ ID NO:6.

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21. The substantially purified polypeptide of claim 17 comprising an amino acid sequence of SEQ ID NO:9 or SEQ ID NO:11.

5 22. A method for expressing a human cyclooxygenase-3 protein in a recombinant host cell, comprising the steps of:

(a) introducing an expression vector capable of encoding a human cyclooxygenase-3 protein into a cell; and

10 (b) culturing the cells under conditions that allow expression of the human cyclooxygenase-3 protein from the expression vector.

23. An antibody that selectively binds to a polypeptide
15 comprising an amino acid sequence having at least 70% identity to SEQ ID NO:4 or SEQ ID NO:6.

24. A kit comprising a nucleic acid probe that selectively hybridizes to a nucleic acid molecule
20 encoding a polypeptide having at least a 80% sequence identity to SEQ ID NO:4 or SEQ ID NO:6.

25. A kit comprising an antibody that selectively binds to a polypeptide comprising an amino acid sequence having at
25 least 70% sequence identity to SEQ ID NO:4 or SEQ ID NO:6.

26. A kit comprising a polypeptide that has an amino acid sequence having at least 70% identity to SEQ ID NO:4 or SEQ ID NO:6, an agent that is more potent at inhibiting human
30 cyclooxygenase-3 activity than either cyclooxygenase-1 or -2, a substrate for cyclooxygenases, and a means to detect the cyclooxygenase activity.

27. The kit of claim 26, wherein the agent that is more potent at inhibiting human cyclooxygenase-3 activity than either cyclooxygenase-1 or -2, is selected from acetaminophen, phenacetin, dipyrrone, Aspirin, diclofenac, or ibuprofen.

28. The kit of claim 26, wherein the substrate for cyclooxygenases is arachidonic acid.

29. The kit of claim 26, wherein the substrate for cyclooxygenases comprises arachidonic acid coupled with a reducing agent cosubstrate that is chromagenic, fluorogenic, or capable of generating luminescent when catalyzed by the peroxidase activity of cyclooxygenases.

30. A method of detecting a nucleic acid molecule of a human cyclooxygenase-3 gene, comprising the steps of:

(a) contacting a test sample with a nucleic acid probe that hybridizes under stringent conditions to the nucleic acid molecule encoding a polypeptide comprising an amino acid sequence having at least a 70% identity to SEQ ID NO:4 or SEQ ID NO:6, or the complementary sequence thereof; and

(b) detecting the probe-nucleic acid molecule complex.

31. A method of detecting a human cyclooxygenase-3 protein, comprising the steps of:

(a) contacting a test sample with an antibody that selectively binds to a polypeptide comprising an amino acid sequence having at least 70% identity to SEQ ID NO:4 or SEQ ID NO:6; and

(b) detecting the protein-antibody complex.

32. A method of determining human cyclooxygenase-3 activity, comprising the steps of:

- 5 a) incubating a test sample with an agent that is more potent at inhibiting cyclooxygenase-3 than either cyclooxygenase-1 or -2;
- b) exposing a substrate for cyclooxygenase to the test sample;
- 10 c) determining the cyclooxygenase activity of the test sample and comparing it with that of a control wherein the test sample is only exposed to the substrate for cyclooxygenase but not to the agent that is more potent at inhibiting cyclooxygenase-3 than either
- 15 cyclooxygenase-1 or -2.

33. The method of claim 32, wherein the agent that is more potent at inhibiting cyclooxygenase-3 than either cyclooxygenase-1 or cyclooxygenase-2 is selected from
20 acetaminophen, phenacetin, dipyron, Aspirin, diclofenac, or ibuprofen.

34. The method of claim 32, wherein the cyclooxygenase activity of the test sample is determined by the amount of
25 prostanoids produced from the substrate arachidonic acid.

35. The method of claim 32, wherein the cyclooxygenase activity of the test sample is determined by the amount of prostanoids selected from prostaglandin D₂, prostaglandin E₂,
30 prostaglandin F_{2α}, prostaglandin I₂, or thromboxane A₂, and

the prostanoids are produced from the substrate arachidonic acid.

36. The method of claim 32, wherein the cyclooxygenase
5 activity of the test sample is determined by the amount of oxygen consumption in the presence of the substrate.

37. The method of claim 32, wherein the cyclooxygenase
activity of the biological sample is determined by the
10 peroxidase activity associated with the cyclooxygenase.

38. The method of claim 37, wherein the peroxidase activity
associated with the cyclooxygenase is determined using a
reducing agent cosubstrate that is chromagenic, or
15 fluorogenic.

39. The method of claim 38, wherein the reducing agent
cosubstrate is homovanillic acid or N,N,N',N' -
tetramethylphenylenediamine (TMPD).
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40. The method of claim 37, wherein the peroxidase activity
associated with the cyclooxygenase is determined by a
luminescence assay.

25 41. The method of claim 40, wherein the luminescence assay
is a real-time luminescence assay involving luminol
reduction.

42. A method of identifying variations in human
30 cyclooxygenase-3 gene sequences in a sample, comprising the
steps of:

- (a) isolating a human cyclooxygenase-3 polynucleotide from the sample; and
- (b) sequencing the human cyclooxygenase-3 polynucleotide to detect alterations in the gene sequence.

5 43. A method for reducing human cyclooxygenase-3 levels in a cell, comprising contacting the cell with a therapeutically effective amount of a composition that decreases the expression of a cyclooxygenase-3 in the cell.

10 44. The method of claim 43 wherein the composition comprises an antisense nucleic acid or siRNA molecule specific for a human cyclooxygenase-3 gene and wherein the antisense nucleic acid or siRNA molecule specifically suppresses human cyclooxygenase-3 gene expression.

15 45. A method of evaluating the mechanism of action of an analgesic/antipyretic drug in a cell, comprising the steps of:

- (a) administering to the cell an effective amount of a composition that increases or decreases the expression or activity of a human cyclooxygenase-3 in the cell;
- (b) administering to the cell a therapeutically effective amount of the analgesic/antipyretic drug;
- (c) measuring a therapeutic effect of the analgesic/antipyretic drug on the cell, and
- 25 (d) comparing the therapeutic effect with that of a control.

46. A method of identifying a compound that alters prostanoid synthesis catalyzed by a human cyclooxygenase-3, comprising the steps of:

- 5 a) contacting a human cyclooxygenase-3 protein, or a polypeptide comprising an active fragment of the human cyclooxygenase-3 protein, with a test compound and with a substrate for cyclooxygenase;
- 10 b) determining the cyclooxygenase activity in step(a), and comparing it with that of a control wherein the human cyclooxygenase-3 protein, or the polypeptide is exposed to the substrate for cyclooxygenase and is not exposed to the test compound.

47. The method of claim 46, wherein the human
15 cyclooxygenase-3 protein or polypeptide is isolated or substantially purified.

48. The method of claim 46, wherein the human
20 cyclooxygenase-3 protein or polypeptide is part of an isolated membrane preparation.

49. The method of claim 46, wherein the human
cyclooxygenase-3 protein or polypeptide is expressed from a recombinant host cell.

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50. The method of claim 46, wherein the cyclooxygenase activity is determined by the amount of prostanoids produced from the substrate arachidonic acid.

30 51. The method of claim 50, wherein the cyclooxygenase activity is determined by the amount of prostanoids selected from prostaglandin D₂, prostaglandin E₂,

prostaglandin $F_{2\alpha}$, prostaglandin I_2 , or thromboxane A_2 , and the prostanoids are produced from the substrate arachidonic acid.

5 52. The method of claim 46, wherein the cyclooxygenase activity of the biological sample is determined by the amount of oxygen consumption in the presence of the substrate for cyclooxygenase.

10 53. The method of claim 46, wherein the cyclooxygenase activity is determined by the peroxidase activity associated with the cyclooxygenase.

15 54. The method of claim 53, wherein the peroxidase activity associated with the cyclooxygenase is determined using a reducing agent cosubstrate that is chromagenic, or fluorogenic.

20 55. The method of claim 54, wherein the reducing agent cosubstrate is homovanillic acid or N,N,N',N' - tetramethylphenylenediamine.

25 56. The method of claim 53, wherein the peroxidase activity associated with the cyclooxygenase is determined by a luminescence assay.

57. The method of claim 56, wherein the luminescence assay is a real-time luminescence assay involving luminol reduction.

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58. The method of claim 46 further comprising the step of testing whether the test compound changes the cyclooxygenase activity of another cyclooxygenase enzyme.

5 59. The method of claim 58, wherein the other cyclooxygenase is selected from a human cyclooxygenase-1 or a human cyclooxygenase-2.

60. A method of identifying a compound that binds to a
10 human cyclooxygenase-3 protein, comprising the steps of:
(a) incubating a test compound with the human cyclooxygenase-3 protein or an active fragment thereof, and a labeled ligand for the human cyclooxygenase-3 protein;
15 (b) separating the human cyclooxygenase-3 protein or an active fragment thereof from unbound labeled ligand; and
(c) identifying a compound that inhibits ligand binding to the human cyclooxygenase-3 by a reduction in the amount of labeled ligand binding to the human cyclooxygenase-3
20 or an active fragment thereof.

61. The method of claim 60, wherein said human cyclooxygenase-3 protein or an active fragment thereof is isolated or substantially purified.

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62. The method of claim 60, wherein said human cyclooxygenase-3 protein or an active fragment thereof is part of an isolated membrane preparation.

30 63. The method of claim 60, wherein said human cyclooxygenase-3 protein or an active fragment thereof is expressed from a recombinant host cell.

64. The method of claim 60, wherein said labeled ligand for
the human cyclooxygenase-3 protein is selected from
acetaminophen, phenacetin, dipyrrone, Aspirin, diclofenac,
5 or ibuprofen.

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